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EXAMINER

HUTSON, RICHARD G

ART UNIT PAPER NUMBER

1652

DATE MAILED: 08/26/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/898,238

Applicant(s)

WACKETT ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-10, 17, 18 and 24-27 is/are pending in the application.
- 4a) Of the above claim(s) 17 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 5-10 and 24-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 7/3/2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 6) ☐ Other:

DETAILED ACTION

Claims 5-10, 17, 18 and 24-27 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 5-10 and 24-27 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the inventions as claimed can be readily evaluated in one search without placing undue burden on the examiner. Applicants argument is not found persuasive because while the searches for the each of the groups overlap, they are not coextensive. For example, search of Group II would require search of subclass 435/18, a search of which would be unnecessary the search of the elected group I.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17 and 18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

Priority

Applicants amendment of the first line of the specification to state that this application is a division of U.S. Patent Application Serial No. 08/546,793, filed on October 23, 1995 (pending), which is incorporated herein by reference is acknowledged. It is further noted that U.S. Patent Application Serial No. 08/546,793

has issued as U.S. Patent Number 6,284,522. The specification should be amended to reflect this.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892 or PTO-1449, they have not been considered.

Applicants filing of information disclosures, paper no. 4, filed 4/3/2002 is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities: As discussed above, U.S. Patent Application Serial No. 08/546,793 has issued as U.S. Patent Number 6,284,522. The specification should be amended to reflect this.

Appropriate correction is required.

Claim Objections

Claim 7 is objected to because of the following informalities:

Claim 7 recites "(SEQ. ID NO: 2)". The "period" after "SEQ" is not consistent with the other references to "SEQ ID NOs: used in the claims and specification. It is suggested that this period be deleted such as "(SEQ ID NO: 2)".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 9, 10, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 are indefinite in that they are incomplete since they depend from cancelled claims 1 and 3, respectively.

Claim 5, 25 and 27 are indefinite in that they are drawn to an isolated and purified protein and a biologically active derivatives thereof that convert atrazine to hydroxyatrazine. The claim is indefinite in that it is unclear as to applicants intent in the limitation "wherein the protein comprises an amino acid sequence encoded by a DNA molecule having a complement that hybridizes to a DNA having the sequence shown in Figure 6 (SEQ ID NO: 1)..." Applicants limitation appears to only be directed to "the protein" (i.e. an isolated and purified protein and not to the biologically active derivatives thereof, hence the claim is interpreted as encoding any biologically active derivative of the described protein, that convert atrazine to hydroxyatrazine, which reads on any

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protein that converts atrazine to hydroxyatrazine. Further the recitation "isolated and purified protein and a biologically active derivatives thereof that convert atrazine to hydroxyatrazine..." is indefinite in that it is not clear if the limitation "...that convert atrazine to hydroxyatrazine..." is intended to be a limitation of the biologically active derivatives or both the derivatives and the proteins that the derivatives are derivatives thereof.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 6, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5, 6, 25 and 27 are directed to all possible proteins having a molecular weight of about 245 kilodaltons that convert atrazine to hydroxyatrazine (claim 5), wherein said protein is a homotetramer (claim 6), and all possible biologically active derivatives that convert atrazine to hydroxyatrazine, of a protein that comprises an amino acid sequence that either hybridizes to the sequence shown in Figure 6 under the defined stringent hybridization conditions (claim 25) or an amino acid sequence that is greater than about 80% identical to SEQ ID NO: 2 (claim 27). Further claims 25 and 27 are directed to all possible proteins that comprise an amino acid sequence that either

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hybridizes to the sequence shown in Figure 6 under the defined stringent hybridization conditions (claim 25) or an amino acid sequence that is greater than about 80% identical to SEQ ID NO: 2 (claim 27), wherein the claimed proteins have no defined functional/activity limitation (See above 112 second paragraph rejection of claims 25 and 27).

The specification, however, only provides a single representative species isolated from *Pseudomonas* sp. Strain ADP, having the amino acid sequence of SEQ ID NO: 2, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of the claimed proteins by any identifying structural characteristics or properties other than the activity recited in claims 5, 6, 25 and 27, for which no predictability of structure is apparent. The mere structural limitation of having a molecular weight of 245 kilodaltons and being a homotetramer is insufficient to adequately describe the claimed genus structurally. Further in claims 25 and 27, while applicants recite an activity for the biologically active derivatives thereof, the claimed derivatives have no defined structure. While claims 25 and 27 are further drawn to a genus of proteins which are structurally defined as they relate to SEQ ID NO: 1 or 2, these genres of proteins (of claims 25 and 27) are not defined functionally (See above 112 second paragraph rejection of claims 25 and 27).

Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full,

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clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5, 6, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein that comprises an amino acid sequence that either hybridizes to the sequence shown in Figure 6 under the defined stringent hybridization conditions, or a protein that comprises an amino acid sequence that has greater than 80% sequence identity to SEQ ID NO: 2, wherein each protein converts atrazine to hydroxyatrazine, does not reasonably provide enablement for any biologically active derivative that converts atrazine to hydroxyatrazine, or any protein that converts atrazine to hydroxyatrazine, wherein the protein has a molecular weight of about 245 kilodaltons and is a homotetramer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

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the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5, 6, 25 and 27 are so broad as to encompass any protein having a molecular weight of about 245 kilodaltons that converts atrazine to hydroxyatrazine (claim 5), wherein said protein is a homotetramer (claim 6), and any possible biologically active derivatives, of a defined protein, that converts atrazine to hydroxyatrazine, or any protein that comprises an amino acid sequence that either hybridizes to SEQ ID NO: 1, under the defined stringent hybridization conditions (claim 25) or any protein which comprises an amino acid sequence that is greater than about 80% identical to SEQ ID NO: 2 (claim 27).

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims, including those proteins which are merely described as they structurally relate to SEQ ID NOs: 1 and 2, or those functional protein derivatives with no structural limitations. Claims 5 and 6 while defined functionally are not adequately defined structurally. The biologically active derivatives of claims 25 and 27 rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the claimed enzymes, while the remaining portion of the genus of these claims is defined structurally, but is not defined functionally. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the

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protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that the atrazine chlorohydrolase having the amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any atrazine chlorohydrolase because the specification does not establish: (A) regions of the protein structure which may be modified without effecting atrazine chlorohydrolase activity; (B) the general tolerance of atrazine chlorohydrolases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a atrazine chlorohydrolase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions

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would be acceptable to retain atrazine chlorohydrolase activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those proteins or biologically active derivatives thereof, of the claimed genus having atrazine chlorohydrolase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any atrazine chlorohydrolase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 5-7, 9, 10, and 24-27 are rejected under 35 U.S.C. 102(a) as being anticipated by Mandelbaum et al. (Applied and Environmental Microbiology, Vol 61, No. 4, pages 1451-1457, Apr. 1995, See IDS) as evidenced by DeSouza et al. (Journal of Bacteriology, Vol 178, No. 16, pages 4894-4900, Aug. 1996)

Mandelbaum et al. teach the isolation and characterization of a *Pseudomonas* sp. that converts atrazine to hydroxyatrazine. Specifically Mandelbaum et al. teach the preparation of cell extracts of *Pseudomonas* sp. strain ADP which converted atrazine to hydroxyatrazine. The preparation of cell extracts of *Pseudomonas* sp. as taught by Mandelbaum et al. constitutes the "isolation and purification" of those enzymes and proteins in the cell extract. This "isolated and purified" cellular extract taught by Mandelbaum et al. comprises the claimed atrazine chlorohydrolase and thus anticipates the rejected claims. It is acknowledged that Mandelbaum et al. do not teach that the enzyme, which is comprised within the taught cellular extract, has a molecular weight of 245 kilodaltons, is a homotetramer, or has an amino acid sequence of SEQ ID NO: 2, which is encoded by SEQ ID NO: 1. Each of these properties are inherent to the enzyme which is in the cellular extract taught by Mandelbaum et al. as evidenced by DeSouza et al. DeSouza et al. teach that their laboratory (which is the same as Mandelbaum et al.) isolated and identified a bacterial culture, as *Pseudomonas* sp. strain ADP, which degraded atrazine DeSouza et al. additionally cloned, characterized and expressed a DNA fragment from the strain ADP that confers atrazine dechlorination ability on *E. coli* DH5 α . DeSouza et al. further teach that the encoded enzyme is a

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homotetramer having a molecular weight of 245 kilodaltons and comprises the amino acid sequence of instantly disclosed SEQ ID NO: 2, which is encoded by instantly disclosed SEQ ID NO: 1. Based on the facts that the groups of Mandelbaum et al. and DeSouza et al. are part of the same laboratory, and DeSouza et al. references Mandelbaum et al. and the taught *Pseudomonas* sp. strain ADP as the source of the protein and gene they describe, it is believed that the protein taught by DeSouza et al. is that which is comprised in the cellular extract of Mandelbaum et al. which is responsible for the atrazine degradation by said extract.

Thus, while it is acknowledged that DeSouza et al. is not available as prior art, DeSouza et al. is used as evidence that the cellular extract taught by Mandelbaum et al. comprised the claimed protein. Thus claims 5-7, 9, 10, and 24-27 are anticipated by Mandelbaum et al. as evidenced by DeSouza et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mandelbaum et al. (Applied and Environmental Microbiology, Vol 61, No. 4, pages 1451-1457, Apr. 1995, See IDS) and Kennedy (See IDS).

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As discussed above, Mandelbaum et al. teach the preparation of cell extracts of *Pseudomonas* sp. strain ADP which converted atrazine to hydroxyatrazine, said cell extracts comprising the atrazine chlorohydrolase having the amino acid sequence of SEQ ID NO: 2.

Kennedy teaches principles of enzyme immobilization, specifically the immobilization of hydrolases for use in waste treatment (see page 292).

One of ordinary skill in the art would have been motivated to further isolate and purify the atrazine chlorohydrolase that Mandelbaum et al. was in possession of and immobilize the enzyme on a support such that it could be used as system to remove the pesticide atrazine from the environment. The motivation to use the purified enzyme for such purposes comes from Mandelbaum et al. who teach that the presence of atrazine in soil needs to be removed and the identified activity provides a good means for doing so. The reasonable expectation of success comes from Kennedy who teach the industrial use of other immobilized hydrolases in waste treatment processes. Thus claim 8 is made obvious by Mandelbaum et al. and Kennedy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax

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phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read "Richard Hutson", with a long horizontal line extending to the right.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
August 23, 2002